Epilepsy & Behavior 52 (2015) 133–142

Contents lists available at ScienceDirect

Epilepsy & Behavior

journal homepage: www.elsevier.com/locate/yebeh

A randomized controlled multimodal behavioral intervention trial for improving antiepileptic drug adherence

Amir H. Pakpour [a,*], Maryam Gholami [b], Ravanbakhsh Esmaeili [c], Seyed Abolhasan Naghibi [c], John A. Updegraff [d], Gerard J. Molloy [e], Stephan U. Dombrowski [f]

[a] Social Determinants of Health Research Center, Qazvin University of Medical Sciences, Qazvin, Iran
[b] Department of Health Psychology, Freie Universität Berlin, Habelschwerdter Allee 45, 14195 Berlin, Germany
[c] Mazandaran University of Medical Sciences, Sari, Iran
[d] Department of Psychological Sciences, Kent State University, USA
[e] School of Psychology, National University of Ireland, Galway, Ireland
[f] School of Natural Sciences, University of Stirling, Cottrell Building, FK9 4LA Stirling, UK

ARTICLE INFO

Article history:
Received 6 July 2015
Revised 26 August 2015
Accepted 30 August 2015
Available online 28 September 2015

Keywords:
Epilepsy medical adherence
Motivational interviewing
Planning
Self-monitoring

ABSTRACT

Purpose: Medication nonadherence is one of the most important reasons for treatment failure in patients with epilepsy. The present study investigated the effectiveness of a multicomponent intervention to improve adherence to antiepileptic drug (AED) medication in patients with epilepsy.
Methods: In a prospective, randomized multicenter trial, three sessions of face-to-face motivational interviewing (MI) in combination with complementary behavior change techniques were compared with standard care. Motivational interviewing prompted change talk and self-motivated statements from the patients, planning their own medication intake regimen and also identifying and overcoming barriers that may prevent adherence. Participants were provided with calendars to self-monitor their medication taking behavior. A family member and the health-care team were invited to attend the last session of MI in order to improve the collaboration and communication between patients, their caregiver or family member, and their health-care provider. At baseline and 6-month follow-up, psychosocial variables and medical adherence were assessed.
Results: In total, 275 participants were included in the study. Compared with the active control group, patients in the intervention group reported significantly higher medication adherence, as well as stronger intention and perceptions of control for taking medication regularly. The intervention group also reported higher levels of action planning, coping planning, self-monitoring, and lower medication concerns.
Conclusions: This study shows that MI can be effective in clinical practice to improve medication adherence in patients with epilepsy. It also provides evidence that combining volitional interventions, including action planning, coping planning, and self-monitoring with motivational interviewing can promote the effectiveness of the medical treatments for epilepsy by improving adherence.

1. Introduction

Epilepsy is one of the most common neurological disorders, with 4 to 10 in every 1000 people affected worldwide. The overall incidence of epilepsy is around 50 per 100,000 people per year (range: 40 to 70 per 100,000 people per year) in industrialized countries and 100 to 190 per 100,000 people per year in developing countries [1]. In Iran, the prevalence of epilepsy has been estimated to be 18 per 1000 people in the population [2].

Approximately 60% of patients with epilepsy could have full control over their seizures with antiepileptic drugs (AEDs) if they took their medication as prescribed [3]. However, nonadherence is one of the most important reasons for treatment failure in these patients [4], as 30% to 50% of adults with epilepsy adhere poorly to their AED treatment schedules [5–9]. However, continuous objective measures suggest even higher rates of nonadherence. For example, two studies using the Medical Events Monitoring System (MEMS)—a pill bottle with an electronic cap that records each time the bottle is opened—found that 76% of doses were taken overall [10], and 48% of patients took one-third or fewer of the prescribed AED doses [11].

Poor adherence affects important treatment outcomes such as numbers of hospital admissions, inpatient treatment days, emergency room

Abbreviations: MI, motivational interviewing; AEDs, antiepileptic drugs; MARS, Medication Adherence Report Scale; BMQ, Beliefs about Medications Questionnaire; PBC, Perceived behavioral control.

* Corresponding author at: Qazvin University of Medical Sciences, Qazvin, Iran. Tel./fax: +98 28 33239259.
E-mail addresses: Pakpour_Amir@yahoo.com, apakpour@qums.ac.ir (A.H. Pakpour).

http://dx.doi.org/10.1016/j.yebeh.2015.08.036
1525-5050/

visits, and health-care costs [12,13]. Nonadherent patients report more uncontrolled seizures leading to greater epilepsy-related morbidity and mortality compared with adherent patients. In addition, nonadherence reduces treatment benefits [14] and can bias assessment of the efficacy of these treatments [15,16].

Medication treatment for epilepsy and other chronic diseases requires patients to merge regimens into daily routines [17]. Although educating patients with epilepsy about medication regimens is critical to treatment [6], additional factors such as sociodemographics or beliefs about epilepsy and medication use are likely to influence treatment adherence [18].

Nonadherence can be either intentional, due to a patient's own choice, or nonintentional, due to forgetting or misunderstanding the prescription and recommendations [19]. According to a Cochrane review [19], behavior change interventions designed to increase medication adherence include simplifying the dosage regimen, combining detailed instructions with counseling, increasing follow-up, sending out reminders, and the use of self-monitoring, rewards, motivational group sessions, and psychological therapy. The review also suggested that education and counseling were effective strategies and behavioral interventions including reminders and implementation intentions had evidence of efficacy in patients with epilepsy.

Most behavior change interventions contain educational and behavioral techniques to improve medical adherence and are usually based on the assumption that participants are motivated to change [20]. However, interventions that take a prescriptive, educational approach may also increase resistance among participants who are not intending to change [21,22]. Motivation to adhere to epilepsy medications has received little research attention.

Motivational interviewing (MI) is a patient-centered clinical strategy that focuses on self-efficacy and personal attitudes towards behavior change. It aims to help individuals solve their ambivalence about change and boost their intrinsic motivation [23,24]. It assesses a client's 'readiness' to change and attempts to enhance motivation for behavior change [25]. It encourages the patient to compare the pros and cons of change and helps in the decision-making prior to education and self-regulatory interventions by enhancing intrinsic motivation [20].

In one study on improving medication adherence in patients with epilepsy, Dilorio et al. [26] provided 5 MI sessions, of which the first session was face to face and the following four sessions were administered

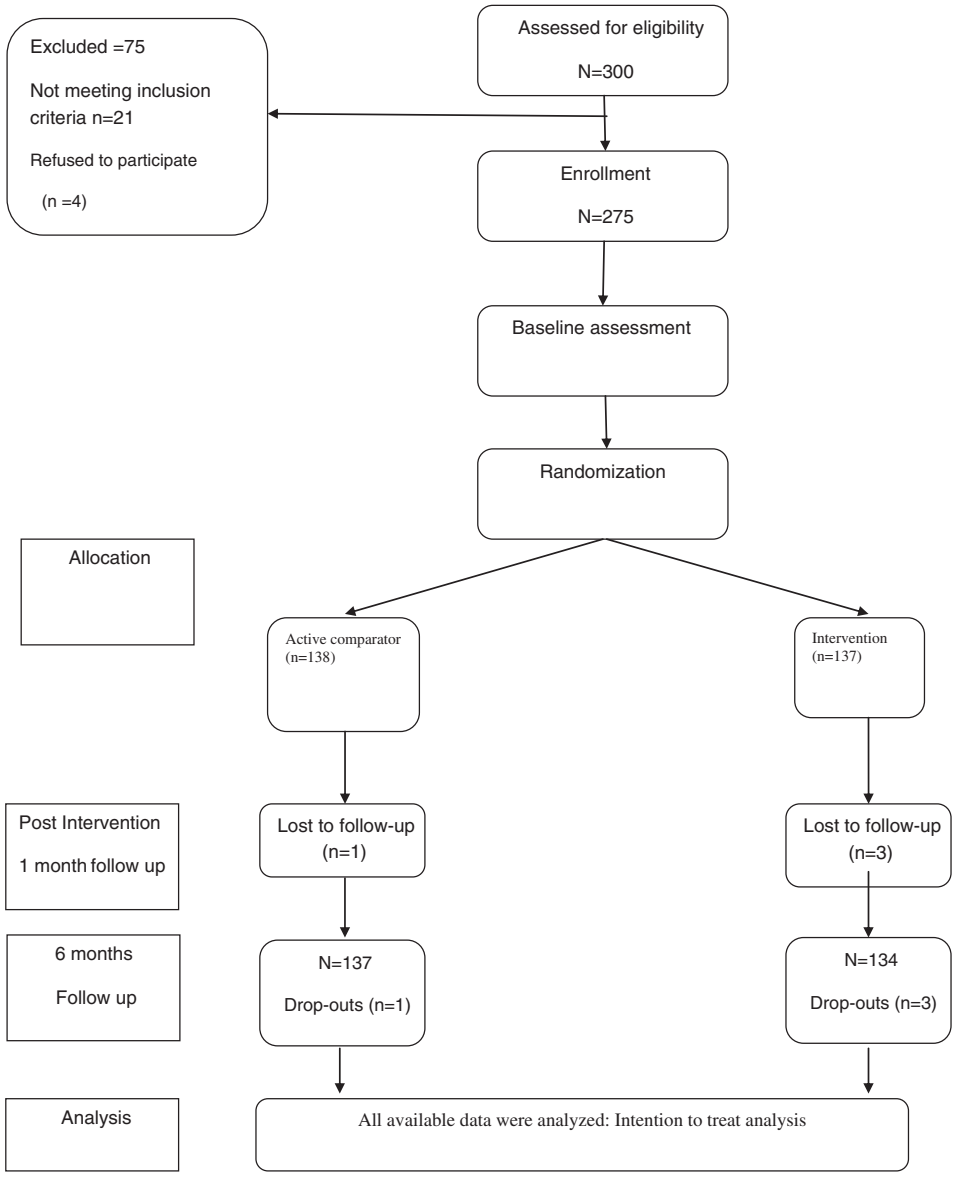

Fig. 1. CONSORT trial flow chart.

by telephone. Patients reported improved adherence over the course of the study. Despite the scarcity of research on implementing MI to improve medical adherence in patients with epilepsy, MI has been used for medication adherence in patient populations with various other medical problems to attempt to resolve ambivalence about medication use and increase medication adherence behaviors [27]. For example, in a study on patients with bipolar disorder, one face-to-face MI session and two follow-ups of MI interventions by phone call were delivered by psychiatric nurse practitioners, which was shown to be an effective treatment approach to improve medication adherence [27].

In the present study, we tested whether a multicomponent intervention to improve adherence to medication could lead to better adherence to AEDs in patients with epilepsy. The intervention, which included motivational interviewing as a core element and included a combination of related and supplementary behavior change techniques [28], was compared with standard care [29] in a randomized controlled trial design. We hypothesized that the active multicomponent intervention would lead to better medication adherence compared with standard care at the follow-up measurement points 3 and 6 months following delivery of the intervention.

2. Experimental procedures

2.1. Design

The study design was a prospective, randomized (1:1 allocation), double blind, multicenter trial among patients with epilepsy. Patients were recruited from 8 neurologic clinics from Qazvin (n = 2) and Tehran (n = 6). The study included two arms, a motivational interviewing intervention and an active standard care comparator. The protocol was approved by the Medical Sciences ethics committee of Qazvin University (February 2014) and was registered on ClinicalTrials.gov (NCT02165306).

2.2. Participants

The patients were recruited nonselectively and consecutively during the period from June 2014 until February 2015. To be eligible for participation, patients had to: (a) have a diagnosis of epilepsy according to the International League Against Epilepsy criteria, (b) be aged 18 years or over, (c) have independence in daily living activities or be responsible for taking their medications, and (d) be prescribed AEDs. Patients were excluded from the study if: (a) they had a presence of a rapidly progressing neurological or medical disorder, (b) they were not prescribed AEDs, (c) they had a diagnosis of an intellectual disability, (d) they had major cognitive impairment (as assessed by the mini–mental state examination <23), or (e) they were not able to read and write Persian.

2.3. Motivational interviewing intervention

The MI intervention was a multifaceted program targeting improved medication adherence behavior and clinical outcomes in patients with epilepsy. Three weekly face-to-face sessions were performed to improve medication adherence [24,30,31]. The MI sessions were delivered individually by a male health psychologist with 10 years of experience working with medication adherence in patients with chronic diseases and 60 h of training of MI in Qazvin and Tehran. During the sessions, the patients were encouraged to express their experiences, values, readiness, and confidence for the behavior change. All sessions were held in a private and quiet setting within a neurologic clinic. Each session lasted for 40 to 60 min. The MI techniques employed to resolve barriers and encourage patients to take medications regularly were open-ended questions, affirmations, reflective statements, and summaries to elicit change talk.

The sessions were conducted in four phases. The facilitator first described the aims of the session, and the patient's motivation and confidence in relation to medication adherence were assessed. In the second phase, the patients were encouraged to express their concerns and barriers about taking medication regularly. The reasons for the reported levels of motivation and confidence were explored, and the facilitator elicited self-motivational statements to foster motivation for medication adherence. If appropriate, patients were invited to consider

Table 1
Demographic and clinical characteristics of the eligible subjects in intervention and active comparator control groups.

	Active comparator (n = 138)	Intervention (n = 137)	p-Value
Age (years)			
Mean (SD)	39.86 (15.01)	41.37 (16.25)	0.40
Sex			0.70
Male	89 (67.2%)	92 (67.2%)	
Female	49 (35.5%)	45 (32.8%)	
Marital status			0.50
Single	62 (44.9%)	63 (46.0%)	
Married	66 (47.8%)	59 (43.1%)	
Divorced/widowed	10 (7.2%)	15 (10.9%)	
Education (years)			
Mean (SD)	7.12 (3.81)	7.03 (4.19)	0.39
Family income ($)			0.62
High (>1000$)	38 (27.5%)	40 (29.2%)	
Intermediate (500–1000$)	72 (52.2%)	64 (46.7%)	
Low (<500$)	28 (20.3%)	33 (24.1%)	
Occupational status			0.59
Employed	43 (31.2%)	38 (27.7%)	
Unemployed	95 (68.8%)	99 (72.3%)	
Time since diagnosis (years)			
Mean (SD)	15.27 (7.38)	14.88 (7.02)	0.37
Treatment regimen			0.59
Monotherapy	101 (73.2%)	37 (26.8%)	
Polytherapy	96 (70.1%)	41 (29.9%)	
Epilepsy type			0.56
Idiopathic	60 (43.5%)	55 (40.1%)	
Cryptogenic	38 (27.5%)	34 (24.8%)	
Symptomatic	40 (29.0%)	48 (35.0%)	
Seizure type			0.91
Focal	64 (46.4%)	60 (43.8%)	
Generalized (convulsions)	39 (28.3%)	38 (27.7%)	
Absence	30 (21.7%)	32 (23.4%)	
Unknown	5 (3.6%)	7 (5.1%)	

Note. SD = standard deviation.

Table 2
The Motivational Interviewing Treatment Integrity (MITI) global measures, behavior counts, and summary scores.

Measurers	Mean ± SD	Minimum	Maximum
Global measures			
Evocation	3.99 (0.65)	2	5
Collaboration	4.28 (0.43)	2	5
Autonomy/support	4.11 (0.55)	1	5
Direction	4.23 (0.67)	2	5
Empathy	4.64 (0.53)	1	5
Behavior counts			
Giving information	0.31 (0.41)	0	
MI—adherent	5.86 (2.98)	1	17
MI—nonadherent	0.91 (1.01)	0	5
Closed questions	13.21 (8.16)	1	31
Open questions	8.38 (4.42)	0	28
Simple reflections	11.82 (7.34)	0	48
Complex reflections	10.62 (6.03)	2	30
Summary scores			
Global spirit rating	4.14 (0.51)	2.19	4.69
Percent complex reflections	52.89 (18.12)	10.83	100.00
Percent open questions	61.49 (16.30)	20.17	100.00
Reflection-to-question ratio	2.67 (2.73)	0.43	18.19
Percent MI adherent	98.07 (6.88)	50.00	100.00

Table 3
Means and standard deviations of all outcome measures in control and intervention groups at baseline and follow-ups.

Variable	Group	Baseline	Month 3	Month 6
BMQ necessary	Control	16.74 (2.11)	16.67 (2.15)	16.29 (2.04)
	Intervention	16.41 (2.27)	19.32 (2.86)	19.26 (2.32)
BMQ concern	Control	12.35 (2.13)	12.92 (1.87)	12.80 (2.07)
	Intervention	12.89 (2.62)	9.71 (2.51)	9.73 (2.17)
BMQ-necessity minus concerns	Control	4.39 (2.11)	3.75 (2.08)	3.49 (2.01)
	Intervention	3.52 (2.37)	9.61 (2.61)	9.53 (2.18)
LSSS	Control	57.87 (21.76)	58.09 (21.75)	60.04 (23.42)
	Intervention	54.62 (22.93)	47.24 (17.41)	42.65 (17.85)
Seizure worry	Control	57.47 (21.36)	56.67 (12.31)	55.03 (12.87)
	Intervention	56.82 (18.48)	64.00 (19.95)	69.92 (11.41)
Overall quality of life	Control	52.85 (17.98)	52.71 (17.97)	52.25 (17.21)
	Intervention	53.75 (19.52)	58.39 (13.04)	62.67 (14.51)
Emotional well-being	Control	55.03 (18.96)	53.91 (16.85)	52.62 (17.79)
	Intervention	52.44 (15.08)	64.12 (17.38)	67.86 (17.43)
Energy/fatigue	Control	50.57 (24.42)	49.42 (14.27)	48.14 (14.56)
	Intervention	52.01 (15.03)	57.03 (16.13)	62.28 (1721)
Cognitive functioning	Control	50.35 (11.33)	47.42 (11.82)	46.03 (12.87)
	Intervention	48.67 (11.80)	56.58 (12.01)	59.92 (11.41)
Medication effects	Control	55.01 (20.81)	54.64 (11.07)	53.57 (11.39)
	Intervention	52.20 (18.91)	62.91 (19.68)	64.86 (19.23)
Social functioning	Control	56.05 (15.66)	55.50 (15.84)	54.78 (16.42)
	Intervention	58.42 (16.61)	67.03 (16.41)	70.17 (17.41)
Overall score	Control	57.43 (14.35)	56.01 (12.12)	55.50 (11.77)
	Intervention	55.75 (14.66)	62.14 (13.21)	65.57 (14.09)
Perceived behavioral control	Control	2.53 (0.86)	2.54 (0.87)	2.49 (0.80)
	Intervention	2.49 (0.79)	2.62 (0.72)	2.61 (0.85)
Intention	Control	2.36 (0.92)	2.34 (0.97)	2.27 (0.87)
	Intervention	2.39 (0.88)	2.72 (0.99)	2.73 (0.95)
Self-monitoring	Control	1.56 (0.65)	1.51 (0.76)	1.49 (0.89)
	Intervention	1.50 (0.53)	1.75 (0.71)	1.76 (0.68)
Action planning	Control	2.08 (0.78)	2.03 (0.78)	1.92 (0.72)
	Intervention	2.11 (0.66)	2.31 (0.69)	2.30 (0.85)
Coping planning	Control	1.95 (0.48)	1.93 (0.54)	1.89 (0.52)
	Intervention	1.96 (0.43)	2.34 (0.87)	2.32 (0.90)
Self-report Behavioural Automaticity Index	Control	1.44 (0.54)	1.40 (0.51)	1.35 (0.49)
	Intervention	1.39 (0.46)	1.63 (0.58)	1.64 (0.56)
MARS	Control	16.34 (4.84)	16.07 (3.69)	15.98 (3.65)
	Intervention	15.67 (3.47)	18.57 (2.21)	18.61 (2.86)

Note. BMQ = Beliefs about Medications Questionnaire, LSSS = Liverpool Seizure Severity Scale, MARS = Medication Adherence Report Scale.

the alternatives to behaviors and beliefs associated with nonadherence and were prompted to find ways for overcoming recognized barriers. The need to maintain medication adherence behavior was reinforced by the facilitator for those patients without any perceived barriers. In the third phase, the pros and cons of medication adherence behavior were discussed. The patients were encouraged to think about the possible future situations in relation to medication adherence. Furthermore, the facilitator and patients collaboratively identified a number of actions for plan behavior change. Participants were encouraged to list those values that might be helpful for medication adherence behavior. The patients also selected their top 3 values and expressed their reason for selecting them. Patients were then invited to create a personal action plan for their actions by specifying where, when, how, and how often they would take medications (action planning), as specified in Michie et al.'s Behavior Change Technique (BCT) Taxonomy [28]. In addition to this, the patients were encouraged to identify the barriers that might interfere with the implementation of their medication adherence plans (barrier identification/problem solving/coping planning) and to specify how to overcome them [28]. Finally, in the fourth phase, patients received a self-monitoring task and a drug diary calendar to help them stick to their plans. This is described as 'Prompt self-monitoring of behaviours' in the BCT Taxonomy [28]. The patients were asked to complete the calendar regularly.

The health-care team, including all GPs and nurses and the patient's family member(s), also received one MI intervention session following the same procedure as for patients. The following issues were discussed separately between health-care providers and patients' family members: the importance of medication adherence in patients, monitoring medication use among patient, the importance of patients–doctor collaboration in developing treatment regimes, allowing patients to describe actual drug taking behavior, and making drug regimens less complex, whenever possible.

2.4. MI integrity/fidelity

In order to ensure the MI sessions were implemented as intended and adequately, integrity and fidelity were evaluated. The Motivational Interview Treatment Integrity (MITI) scale was used to assess integrity to MI in the intervention group [32]. Two trained independent evaluators randomly selected 25% of interviews for scoring. The MI integrity was assessed via the global scores and the behavior counts. The global scores have five variables (i.e., empathy, evocation, collaboration, autonomy/support, and direction) while behavior counts have eight verbal variables (i.e., giving information, asking open-ended and closed-ended questions, providing simple and complex reflections, and making other statements categorized as MI adherent or not). The session's MI fidelity was determined through comparison with recommended standards for global scores, and ratios were calculated [32].

2.5. Standard care (SC)

All participants in both groups received standard care consistent with 'treatment as usual' for patients with epilepsy. This included a one-time session of brief advice to use medications regularly lasting

Table 4
Cross-tabulation of concentration–dose ratio and time in study groups.

	Time 1		Time 2		Time 3	
	Concentration–dose ratio		Concentration–dose ratio		Concentration–dose ratio	
	Within reference range or higher, n (%)	Low or not detectable, n (%)	Within reference range or higher, n (%)	Low or not detectable, n (%)	Within reference range or higher, n (%)	Low or not detectable, n (%)
Active comparator	61 (44.2%)	77 (55.8%)	57 (41.3%)	81 (58.7%)	52 (38.0%)	85 (62.0%)
Intervention	55 (40.1%)	82 (59.9%)	75 (55.1%)	61 (44.9%)	80 (59.7%)	54 (40.3%)

approximately 5 min and delivered by a nurse or physician. Topics typically discussed in these short sessions include coexisting diseases, the history of drug use, current disease, and advice about the health risks of irregular medication use. According to the BCT taxonomy, this would be described as the behavior change technique of providing information on consequences of behavior in general and also for the individual [28].

2.6. Sample size

The aim of this study was to assess whether the multimodal behavioral intervention would be superior to routine counseling for patients with epilepsy in improving medication adherence. Based on our main outcome score (Medication Adherence Self Report Scale [MARS]), sample size was determined based on detecting a small effect ($d = 0.34$) on MARS change scores with a power of 0.85 at $p < 0.05$ [33]. The required sample size was 128 participants per condition, assuming that 10% of the patients would be excluded from the analysis due to study attrition.

2.7. Randomization

All participants gave their written informed consent prior to participation. All eligible participants who agreed to be included in the study completed the baseline measures. Afterwards, an independent researcher who was not involved in the study randomly allocated the patients into either the intervention or active comparator groups. Randomization was performed using a computer-generated code based on random number sequence with stratification by the study sites.

2.8. Measures

The primary outcomes were adherence to prescribed AEDs, assessed with the serum level and the Medication Adherence Report Scale (MARS).

2.8.1. Demographics

Demographic variables assessed included age, gender, monthly family income, marital status, educational status, occupational status, medication regimen, age of onset of epilepsy, epilepsy diagnosis duration, epilepsy type, and seizure type.

2.8.2. The Medication Adherence Report Scale (MARS)

The MARS is composed of five items measured on a five-point Likert scale ranging from 1 (always) to 5 (never). This scale can be split into two scores: nonintentional nonadherence (i.e., item 1: forgetting, possible range: 1–5) and intentional nonadherence (i.e., items 2–5, possible range: 4–20). In addition to this, the total score of the MARS was computed via summing all 5 items (ranging from 5–25). Higher scores indicate higher adherence to medication. The MARS has been used widely in patients with neurologic disorders including epilepsy, and the Persian version has been found to be highly valid and reliable [34].

2.8.3. Serum level

Serum levels of antiepileptic drugs were assessed using a third generation of fluorescence microparticle enzyme immunoassay (MEIA) (Abbott Axsym®, Abbott Laboratories, Abbott Park, IL, USA). All blood samples were taken just before the next usual dose of drug. The therapeutic ranges of AEDs have been reported elsewhere [35]. In order to allow cross comparisons between the study groups, serum concentration–dose ratio was assessed by dividing the measured serum concentration of AEDs (in lmol/L) by the total daily dose (in mg) taken by the patient at that time. Serum levels were categorized into two categories (according to the reference ranges for the laboratory of each AED) including "low or not detectable" (i.e., nonadherent) and "within reference range or higher" (i.e., adherent).

2.8.4. Beliefs about medications

Patient's beliefs about medication use were assessed by the Beliefs about Medications Questionnaire (BMQ) [36]. The BMQ has two parts including specific and general beliefs. We only assessed specific beliefs in line with evidence showing that specific beliefs are associated with medication adherence, whereas general beliefs are not. The BMQ specific has two subscales including necessity of and concern about medication adherence. Each subscale contains five questions, and responses are scored on a five-point Likert scale ranging from 1 (strongly disagree) to 5 (strongly agree). Total scores of each subscale could be computed by summing all items, and scores ranged from 5 to 25. Higher scores in necessity indicate stronger patient's belief about the importance of taking their medication, while higher scores in concern indicate higher patient worries and concern about taking their medications. The Persian version of the BMQ has been tested in patients with type 2 diabetes and showed good validity and reliability [37].

2.8.5. Perceived behavioral control (PBC)

Perceived behavioral control was measured using four items adapted from previous research [34]. The participants rated their responses on a five-point Likert scale from 1 (difficult) to 5 (easy) (e.g., "for me to take regular medication in the future is…"). Internal consistency for this scale was acceptable ($\alpha = 0.93$).

Table 5
The logistic regression model predicting serum level in study groups.

Variables	Month	Serum level	
		OR (CI)	p-Value
Group (intervention vs. control)		1.11 (0.69–1.78)	0.64
Month	3	1.12 (0.70–1.79)	0.62
Intervention vs. control	3	1.35 (1.07–1.71)	0.03
Month	6	1.31 (0.82–2.10)	0.27
Intervention vs. control	6	2.81 (1.44–5.47)	0.002
Age		1.01 (1.00–1.02)	0.04
Gender (male)		1.12 (0.82–1.51)	0.46
Medication dosing regimens (monotherapy)		0.76 (0.45–1.29)	0.27
Time since seizure		1.01 (0.98–1.03)	0.49
Intercept		0.97 (0.63–1.49)	0.89

Table 6
Multiple linear regression models predicting beliefs about medicines, intention, perceived behavioral control, self-monitoring, action planning, coping planning, and medication adherence behavior.

Variable	Month	BMQ specific necessity		BMQ specific concerns		PBC		SM	
		B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
Group (intervention vs. control)		2.90 (0.50)	<0.001	−3.73 (0.57)	<0.001	0.70 (0.14)	<0.001	0.68 (0.12)	<0.001
Month	3	1.79 (0.26)	<0.001	−3.48 (0.34)	<0.001	0.35 (0.07)	<0.001	0.45 (0.06)	<0.001
Intervention vs. control	3	3.15 (0.40)	<0.001	−4.03 (0.48)	<0.001	0.76 (0.11)	<0.001	0.70 (0.08)	<0.001
Month	6	2.70 (0.28)	<0.001	−2.37 (0.29)	<0.001	0.19 (0.07)	<0.009	0.16 (0.06)	0.008
Intervention vs. control	6	2.17 (0.37)	<0.001	−2.49 (0.41)	<0.001	0.60 (0.10)	<0.001	0.40 (0.08)	<0.001
Age		−0.01 (0.01)	0.19	0.07 (0.01)	<0.001	−0.001 (0.003)	0.17	−0.01 (0.002)	<0.001
Gender (male)		−0.07 (0.04)	0.11	1.22 (0.43)	0.005	−0.20 (0.10)	0.04	0.20 (0.08)	0.01
Medication dosing regimens (monotherapy)		−0.07 (0.04)	0.10	0.06 (0.05)	0.29	0.29 (0.11)	0.008	−0.01 (0.01)	0.24
Time since seizure		−1.24 (0.37)	0.01	0.76 (0.47)	0.11	−0.05 (0.01)	0.006	−0.26 (0.08)	0.002
Intercept		17.25 (0.63)	<0.001	17.61 (0.77)	<0.001	4.01 (0.18)	<0.001	4.09 (0.19)	<0.001

Note. BMQ = Beliefs about Medications Questionnaire, PBC = perceived behavioral control, SM = self-monitoring, INT = behavioral intention, AP = action planning, CP = coping planning, BEH = medication adherence behavior, BA = behavioral automaticity.

2.8.6. Behavioral intention

Intention to adhere to medication was assessed by five items adapted from previous research [34]. An example item was "I intend to take regular medication in the future". These items were measured on a five-point scale anchored by completely disagree (1) and completely agree (5). Internal consistency analysis indicated that the measure had adequate reliability ($\alpha = 0.86$).

2.8.7. Self-monitoring

Self-monitoring was measured by three items adapted from previous research [38] (e.g., "During the last week, I have consistently monitored when to take my medications", scored not at all true (1) to exactly true (5)). Cronbach's α for the scale was 0.81 indicating acceptable reliability.

2.8.8. Action planning

Action planning was assessed using four items with a stem: "I have made a detailed plan regarding" followed by "(a) when to take medication", "(b) where to take medication", "(c) how often to take medication", and "(d) how to take medication". All responses were rated on a five-point Likert scale (1 = completely disagree, 5 = completely agree) [34]. The four items had high internal consistency ($\alpha = 0.92$).

2.8.9. Coping planning

Coping planning was assessed by four items with a stem "I have made a detailed plan regarding" followed by "(a) what to do if something interferes", "(b) what to do if I forgot it", "(c) how to motivate myself if I don't feel like it", and "(d) how to prevent being distracted" [34]. All items were scored on five-point Likert scales ranging from 1 (completely disagree) to 5 (completely agree). The four items formed an internally reliable scale ($\alpha = 0.92$).

2.8.10. Behavioral automaticity

Behavioral automaticity was assessed using the Self-Report Behavioural Automaticity Index (SRBAI). The SRBAI has four items which assess automaticity of behavior. This scale has a stem "Behavior X (e.g., medication adherence) is something…" followed by (a) "I do automatically", (b) "I do without having to consciously remember", (c) "I do without thinking", and (d) "I start doing before I realize I'm doing it". Respondents were asked to indicate the extent to which they agreed on a five-point Likert scale ranging from 1 (disagree) to 5 (agree). The Persian/Iranian version of the SRBAI has been adopted in an independent study on patients with epilepsy. There was no difference to the English version. Moreover, the Iranian version of the SRBAI showed good psychometric properties with an adult clinical population. In order to ease comparison, a five-point Likert scale was employed.

2.8.11. Liverpool Seizure Severity Scale (LSSS)

The LSSS is a self-report measure which assesses the severity of a patient's seizures during the past 4 weeks [39]. It contains 12 items that are scored on a Likert scale. Patients who had no seizure for 4 weeks prior to the study score a "zero" while those patients who failed to answer four or more question of the LSSS were regarded as "missing". Individual scores ranged from 0 to 100 with higher scores indicating worsening seizure severity. The Persian version of the LSSS had been translated and culturally adapted prior to the study. The Persian version of the LSSS has been found to be a valid and reliable tool in quantifying seizure severity of patients with epilepsy and detecting changes in seizure severity over time.

2.8.12. Health-related quality of life

Health-related quality of life in patients with epilepsy was assessed using a standard tool, the Quality of Life in Epilepsy—31 inventory (QOLIE-31) [40]. The QOLIE-31 is a self-reported questionnaire with 31 items which cover seven dimensions including seizure worry, overall quality of life, emotional well-being, energy–fatigue, cognitive functioning, medication effects, and social function. All responses ranged from 0 to 100 with higher scores indicating better quality of life. The overall score of the QOLIE-31 could be computed by weighting and summing seven dimension scores. The Persian version of the QOLIE-31 was found to be a reliable measure to assess health-related quality of life in patients with epilepsy [41].

2.9. Statistical analysis

Participant characteristics were summarized using descriptive statistics (mean, standard deviation, frequency). To ensure the equivalence of groups at baseline in terms of clinical and demographic variables, independent t-test for continuous variables and chi-square tests for categorical variables were performed. The magnitude of change over time across study groups was examined by linear mixed models (PROCMIXED) for continuous outcome variables controlling for age, gender, number of medications, and time since seizure. Random effects included study centers and participant number. Mixed modeling is an appropriate technique for unequal numbers of participants at baseline and follow-up. In this analysis, two between-participant effects (between groups and between participants within groups) and three within-participant effects (between times, group by time interactions, and random variation) were included. In this case, a series of separate linear mixed models were evaluated. The analyses were applied in accordance to the intention-to-treat principle. The method of estimation was maximum likelihood with unstructured covariance. All tests and p-values were adjusted for multiple comparisons using the Benjamini–Hochberg procedure. As serum level was a binary outcome, a logistic mixed model was conducted

INT		AP		CP		BEH		BA	
B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
0.53 (0.14)	<0.001	0.39 (0.10)	<0.001	0.52 (0.14)	<0.001	4.05 (0.60)	<0.001	0.64 (0.12)	<0.001
0.38 (0.05)	<0.001	0.23 (0.05)	<0.001	0.45 (0.06)	<0.001	3.25 (0.43)	<0.001	0.50 (0.07)	<0.001
0.47 (0.07)	<0.001	0.39 (0.07)	<0.001	0.52 (0.9)	<0.001	4.60 (0.61)	<0.001	0.74 (0.09)	<0.001
0.05 (0.04)	0.18	0.02 (0.04)	0.052	0.16 (0.05)	0.004	0.60 (0.33)	0.07	0.27 (0.06)	<0.001
0.12 (0.06)	0.03	0.14 (0.06)	0.022	0.22 (0.08)	0.007	1.73 (0.47)	<0.001	0.49 (0.09)	<0.001
0.01 (0.04)	0.80	0.001 (0.002)	0.67	−0.002 (0.004)	0.060	−0.02 (0.015)	0.25	−0.009 (0.003)	0.003
−0.30 (0.14)	0.040	−0.15 (0.09)	0.08	−0.79 (0.13)	<0.001	−0.88 (0.49)	0.07	−0.15 (0.1)	0.12
−0.02 (0.02)	0.23	−0.13 (0.10)	0.17	−0.02 (0.02)	0.22	−0.14 (0.06)	0.03	−0.06 (0.11)	0.53
−0.62 (0.16)	<0.001	−0.01 (002)	0.67	−0.24 (0.14)	0.09	−1.85 (0.54)	<0.001	−0.04 (0.01)	0.001
3.54 (0.24)	<0.001	4.57 (0.15)	<0.001	3.85 (0.22)	<0.001	23.18 (0.86)	<0.001	4.33 (0.17)	<0.001

to assess the intervention effects on the serum level in patient groups. The latter analysis was employed to estimate the odds ratios (OR) for achieving greater than 95% serum level between the two arms. Study centers and participant number were included as random effects, and fixed effects included age, gender, medication regimen, and time since seizure. All statistical analyses were performed using SAS® software (Cary, NC, USA).

3. Results

3.1. Demographic and baseline characteristics

The CONSORT flow diagram shows 275 participants enrolled in the study (Fig. 1). Three hundred patients were approached and checked for eligibility. In total, two hundred and seventy-five patients were randomized to receive intervention and standard care (Fig. 1). At follow-up, 4 patients (1.5%) did not return their questionnaires and were not available for taking blood samples. Patients who dropped out were not significantly different from patients who completed the study. Clinical and demographic characteristics between the two groups were compared and did not differ from each other (Table 1).

3.2. Treatment integrity

The MI quality was assessed using MITI. Mean scores for MITI as well as SDs are shown in Table 2. There was evidence of adherence to the allocated interventions. All MITI summary scores indicated a level of achieving proficiency or competency (Table 2).

3.3. Primary outcomes

Tables 3 and 4 summarize the outcome measures over 6 months.

3.3.1. Medication adherence

Table 3 shows mean scores of MARS at baseline, 3 months, and 6 months in study groups. There was a progressive increase in average MARS in the intervention group, but no change was observed in the standard care group. Patients in the intervention group reported significantly higher medication adherence compared with those in the active comparator group at 3 months ($\beta = 4.6$, $p < 0.001$) and 6 months ($\beta = 1.73$, $p < 0.001$) of follow-ups.

3.3.2. Serum level

Table 5 shows results for estimating the serum level change over repeated visits. The odds ratios of serum level were increased by 1.35 in patients in the intervention group (OR 1.35, 95% CIs: 1.07–1.71, $p = 0.03$) compared with those in the active comparator group at 3 months of follow-up. At the 6-month point, the chance of having patients within reference range or higher were increased by 2.81 in patients in the intervention group (OR 2.81, 95% CIs: 1.44–5.47, $p = 0.002$) compared with those in the active comparator group.

3.3.3. Beliefs about medications

The mean change as well as SD of the BMQ-specific subscales are shown in Table 3. Medication concerns reduced significantly in patients who received prescribed intervention in comparison with those in the active control group at 3 and 6 months of follow-ups ($p < 0.001$) (Table 5). Data on BMQ-necessity are shown in Tables 3 and 6. The MI intervention group yielded a significant increase in BMQ-necessity versus the active comparator group at 3 and 6 months of follow-ups ($p < 0.001$).

3.3.4. Social cognitive variables

There were some significant differences between the groups on the social cognitive variables at 3-month and 6-month follow-ups (Tables 3, 6). In particular, patients in the intervention group reported stronger intention and perceptions of control than patients in the active comparator group for taking medication regularly. Patients in the active comparator group were less likely than patients in the intervention group to report that they had a clear plan for taking medication regularly. In addition to this, patients in the active comparator group significantly reported lower levels of any plan to anticipate and overcome barriers for taking medication regularly. Furthermore, self-monitoring was significantly improved in patients in the intervention group compared with the patients in the active comparator group.

Changes in behavioral automaticity over time occurred in the intervention group, and a significant time by group interaction indicated that this was significantly larger across time than in the active comparator group. In the active comparator group, a nonsignificant decrease of 0.90 ($SD = 0.39$) over time was found.

3.3.5. Seizure severity

Over the 6-month follow-up, there was a statistically significant difference between the intervention and the active comparator groups in seizure severity (Tables 3, 7), with lower scores in the intervention group ($p < 0.05$).

3.3.6. Health-related quality of life

At baseline, QOLIE-31 domain scores were generally well matched between study groups (Tables 3 and 7). At 6 months, no significant changes from baseline in any domain were evident in the active comparator group. On the other hand, in patients receiving intervention, the mean changes from baseline were statistically significant in all domains as well as the overall score (Table 7).

Table 7
Multiple linear regression models predicting health-related quality of life and seizure severity.

Variable	Month	SW		OQOL		EW		EN/FA	
		B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
Group (intervention vs. control)		14.75 (4.35)	<0.001	11.62 (3.57)	<0.001	6.00 (3.08)	0.05	14.58 (3.92)	<0.001
Month	3	13.10 (1.98)	<0.001	8.92 (1.61)	<0.001	5.17 (1.35)	0.002	10.28 (1.81)	<0.001
Intervention vs. control	3	14.75 (4.35)	<0.001	9.53 (2.28)	<0.001	7.50 (1.91)	0.001	11.71 (2.57)	<0.001
Month	6	5.92 (1.68)	0.005	4.28 (1.33)	0.001	2.32 (0.099)	0.020	5.28 (1.37)	<0.001
Intervention vs. control	6	6.57 (2.38)	<0.001	4.75 (1.88)	0.01	3.57 (1.41)	0.019	5.57 (1.944)	0.004
Age		−0.57 (0.14)	<0.001	−0.67 (0.10)	<0.001	−0.45 (0.09)	<0.001	−0.79 (0.12)	<0.001
Gender (male)		0.36 (0.34)	0.67	−4.18 (3.33)	0.21	−3.97 (3.13)	0.20	−9.98 (3.79)	0.008
Medication dosing regimens (monotherapy)		−0.45 (0.39)	0.47	−0.89 (0.44)	0.04	2.82 (2.43)	0.41	−2.10 (0.50)	<0.001
Time since seizure		1.88 (1.82)	0.71	−0.67 (0.10)	<0.001	−1.65 (0.41)	<0.001	−1.49 (1.17)	0.72
Intercept		101.97 (7.73)	<0.001	69.51 (5.68)	<0.001	98.50 (5.26)	<0.001	90.93 (6.41)	<0.001

Note SW = seizure worry, OQOL = overall quality of life, EW = emotional well-being, EN/FA = energy–fatigue, CF = cognitive functioning, ME = medication effects, SF = social functioning, OS = Overall score, LSSS = Liverpool Seizure Severity Scale.

4. Discussion

Our results illustrate that at follow-up, patients in the intervention group reported significantly better medication adherence, stronger intention, and greater perceptions of control for taking medication regularly compared with the active comparator group. Moreover, the intervention group reported higher levels of action planning, coping planning, and self-monitoring. Furthermore, we observed fewer medication concerns and enhanced medication taking automaticity in patients who received the intervention compared with the active comparator group.

As Gollwitzer points out, there are two phases for performing a given behavior [42] such as adhering to medication: (1) the motivational phase in which cognitions about the target behavior help patients to make a decision to act (i.e., deciding to adhere to medication), and (2) the volitional phase in which patients commit to act. According to this conceptualization, the volitional phase reflects the implementation of a patient's decisions. In this study, a combination of motivational and volitional interventions were used in clinical practice to support patients with epilepsy in order to enhance their medication adherence. Motivational interviewing is one form of a motivational intervention which can help to facilitate decision-making in patients, while a volitional intervention (including action planning, coping planning, and self-monitoring) can help patients to commit themselves to change behavior.

Motivational interviewing sessions stimulate a patient's self-evaluation of readiness to change. It is important that the major factors that have an impact on medication adherence be addressed in the process of MI, such as beliefs about medication, the patient's concerns, and relationship with the provider. For example, in a study by McKenzie and Chang [27], patients who initially described themselves as having poor adherence and negative beliefs about taking medications were able to improve their self-efficacy, motivation to change, and medication adherence.

It has been shown that MI can draw the participant's attention towards reasons of poor medication adherence such as side effects. On the other hand, MI seems effective in improving patients' motivation to communicate these problems with their health-care provider [20,27]. For example, in a randomized controlled trial by Brown and Miller, it was found that those patients who had a received MI became more motivated for medical adherence and also had a better prognosis [43].

Motivational interviewing is a technique which increases people's motivation to adhere, but does not explicitly provide the skills to carry out the steps needed for adherence. In contrast, volitional interventions provide the skills needed to adhere but rely on participants already having the motivation to adhere. The substantial improvement in adherence seen in this study of our combined MI and volitional interventions is evidence of the promise of using these two approaches together. It is necessary to conduct additional similar studies in order to find the best combination of intervention components as well as the length and frequency of such sessions in order to improve the efficiency and feasibility of MI interventions.

A large body of literature underscores the importance of family involvement in illness management [44,45]. A pilot study, which included caregivers in MI sessions for motivating asthma medication adherence in adolescents [20], found that both caregivers and patients reported higher adherence and quality of life. Therefore, future interventions should consider explicitly incorporating family members or other social supports into study designs and, in particular, intervention protocols and outcome assessment in order to optimize approaches to improve adherence and health outcomes for patients and those in their immediate social environment.

While this study showed greater adherence in the intervention group than in the standard care group, the design did not allow for the identification of the most impactful component in the intervention. Indeed, each of the elements of the intervention was included because they were expected to contribute to greater adherence. Future research could benefit by identifying the components of the intervention which have the strongest effects on adherence, as well as the beliefs or skills which mediate the influence of those components on adherence. This will allow refinement of the intervention approach and reduce any unnecessary or unhelpful content. Future studies should also investigate whether a combination of MI with volitional interventions in other groups of patients can improve medical adherence in other domains such as diabetes or asthma.

In this study, the effectiveness of a multimodal intervention on medication adherence was assessed in a relatively short time (i.e., six months). Future studies should also investigate longer term effectiveness of this intervention on improving patients with epilepsy. Despite this fact, the multimodal intervention had consistent and sizable effects on medication adherence as well as patients' quality of life. Future studies are needed to investigate the effectiveness and cost-effectiveness of this kind of intervention on medication adherence in other cultures. In Iran, as a developing country, patients with epilepsy do not receive any considerable intervention for their medication regimens. Neurologic clinics do not consider preventive care (i.e., medication adherence and then seizure prevention) with the same emphasis as acute care. On the other hand, Iranian patients often value attentive relationships with their physicians. Therefore, they expect that their physicians would spend more time listening to their health stories and discuss their health problems in detail. The intervention described in the present study provided an opportunity for patients in the intervention group to build better relationships with their physicians, and patients often received the intervention enthusiastically for this reason. Moreover, this study involved a patient's significant others (i.e., family and caregivers) to improve medication adherence for patients in the intervention group. Thus, the involvement of family and caregivers also synergized with the multimodal behavioral intervention in medication adherence. Involving caregivers and health providers in MI sessions

CF		ME		SF		OS		LSSS	
B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value	B (SE)	p-Value
12.26 (4.92)	0.01	7.40 (4.72)	0.11	16.45 (2.95)	<0.001	8.61 (3.12)	0.18	−14.02 (2.87)	<0.001
12.81 (2.42)	<0.001	8.92 (1.68)	<0.001	11.75 (1.63)	<0.001	13.39 (1.95)	<0.001	−8.66 (1.51)	<0.001
17.45 (3.42)	<0.001	10.35 (2.38)	<0.001	12.96 (2.31)	<0.001	9.62 (2.47)	0.03	−10.84 (2.14)	<0.001
3.90 (1.12)	<0.001	3.21 (1.11)	0.004	3.14 (1.03)	0.002	3.09 (1.09)	0.008	−2.29 (1.20)	0.058
4.62 (1.59)	<0.001	4.28 (1.57)	0.006	3.85 (1.46)	0.009	3.51 (1. 68)	<0.001	−4.24 (1.70)	<0.013
−0.62 (0.15)	<0.001	−0.18 (0.14)	0.23	−0.46 (0.09)	<0.001	−0.28 (0.05)	0.11	0.51 (0.08)	<0.001
−10.71 (4.91)	0.03	−9.42 (4.93)	0.056	3.66 (2.85)	0.200	−3.31 (2.85)	0.006	1.60 (1.30)	0.54
−0.48 (0.65)	0.45	−0.44 (0.41)	0.500	−4.17 (3.12)	0.18	−3.71 (3.24)	0.12	0.56 (0.34)	0.10
7.12 (5.39)	0.188	−14.68 (5.40)	0.007	−1.61 (0.37)	<0.001	−1.01 (0.21)	0.25	5.40 (2.88)	0.06
67.37 (8.27)	<0.001	63.35 (8.23)	<0.001	89.93 (4.83)	<0.001	72.83 (6.71)	<0.001	61.22 (4.50)	<0.001

could be beneficial in terms of providing support for the patient and facilitating communications over concerns and uncertainties towards prescriptions, thus, improving adherence to drug regimens. Future studies should investigate the exact role of a patient's significant others and the physician–patient relationship in improving medication adherence in patients with epilepsy.

4.1. Conclusion

In conclusion, this study shows that the provision of an intervention based on motivational interviewing can significantly improve the medication adherence of patients with epilepsy, and points to the value of such an intervention for medication adherence in general.

Conflict of interest

The authors declare no conflict of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.yebeh.2015.08.036.

References

[1] Sander JW. The epidemiology of epilepsy revisited. Curr Opin Neurol 2003;16:165–70.
[2] Mohammadi MR, Ghanizadeh A, Davidian H, Mohammadi M, Norouzian M. Prevalence of epilepsy and comorbidity of psychiatric disorders in Iran. Seizure 2006;15:476–82.
[3] Kwan P, Brodie MJ. Early identification of refractory epilepsy. N Engl J Med 2000;342:314–9.
[4] Chen JW, Wasterlain CG. Status epilepticus: pathophysiology and management in adults. Lancet Neurol 2006;5:246–56.
[5] Buck D, Jacoby A, Baker GA, Chadwick DW. Factors influencing compliance with antiepileptic drug regimes. Seizure 1997;6:87–93.
[6] Dilorio C, Shafer PO, Letz R, Henry TR, Schomer DL, Yeager K. Project EASE: a study to591 test a psychosocial model of epilepsy medication management. Epilepsy Behav 2004;5:926–36.
[7] Leppik IE. How to get patients with epilepsy to take their medication. The problem of noncompliance. Postgrad Med 1990;88:253–6.
[8] Sackett D, Snow J. The magnitude of adherence and nonadherence. In: Haynes RB, Taylor DW, Sackett DL, editors. Compliance in health care. Baltimore, MD: Johns Hopkins University Press; 1979. p. 1–18.
[9] Shope JT. Compliance in children and adults: review of studies. Epilepsy Res Suppl 1988;1:23–47.
[10] Cramer JA, Mattson RH, Prevey ML, Scheyer RD, Ouellette VL. How often is medication taken as prescribed? A novel assessment technique. JAMA 1989;261:3273–7.
[11] Buelow JM, Smith MC. Medication management by the person with epilepsy: perception versus reality. Epilepsy Behav 2004;5:401–6.
[12] Davis KL, Candrilli SD, Edin HM. Prevalence and cost of nonadherence with antiepileptic drugs in an adult managed care population. Epilepsia 2008;49:446–54.
[13] Faught E, Duh MS, Weiner JR, Guerin A, Cunnington MC. Nonadherence to antiepileptic606 drugs and increased mortality: findings from the RANSOM study. Neurology 2008;71:1572–1578.
[14] Gordis L. Conceptual and methodologic problems in measuring patient compliance. In: Haynes RB, Taylor DW, Sackett DL, editors. Compliance in health care. Baltimore, MD: Johns Hopkins University Press; 1979. p. 23–45.
[15] Haynes R. Determinants of compliance: the disease and the mechanism of treatment. In: Haynes RB, Taylor DW, Sackett DL, editors. Compliance in health care. Baltimore, MD: Johns Hopkins University Press; 1979. p. 49–52.
[16] Haynes RB, Dantes R. Patient compliance and the conduct and interpretation of therapeutic trials. Control Clin Trials 1987;8:12–9.
[17] Ferrari CM, de Sousa RM, Castro LH. Factors associated with treatment nonadherence in patients with epilepsy in Brazil. Seizure 2013;22:384–9.
[18] Hovinga CA, Asato MR, Manjunath R, Wheless JW, Phelps SJ, Sheth RD, et al. Association of non-adherence to antiepileptic drugs and seizures, quality of life, and productivity: survey of patients with epilepsy and physicians. Epilepsy Behav 2008;13:316–22.
[19] Al-Aqeel S Al-Sabhan J. Strategies for improving adherence to antiepileptic drug 621treatment in patients with epilepsy. Cochrane Database Syst Rev 2011(1) CD008312.
[20] Riekert KA, Borrelli B, Bilderback A, Rand CS. The development of a motivational interviewing intervention to promote medication adherence among inner-city, African-American adolescents with asthma. Patient Educ Couns 2011;82:117–22.
[21] Berg-Smith SM, Stevens VJ, Brown KM, Van Horn L, Gernhofer N, Peters E, et al. A brief motivational intervention to improve dietary adherence in adolescents. The Dietary Intervention Study in Children (DISC) Research Group. Health Educ Res 1999;14:399–410.
[22] Channon S, Smith VJ, Gregory JW. A pilot study of motivational interviewing in adolescents with diabetes. Arch Dis Child 2003;88:680–3.
[23] Borrelli B, Riekert KA, Weinstein A, Rathier L. Brief motivational interviewing as a clinical strategy to promote asthma medication adherence. J Allergy Clin Immunol 2007;120:1023–30.
[24] Miller WR, Rollnick S. Motivational interviewing: helping people change. Guilford Press; 2012.
[25] Corrigan PW. Adherence to anti-psychotic medications and health behavior theories. United Kingdom: Taylor & Francis; 2002.
[26] Dilorio C, Reisinger EL, Yeager KA, McCarty F. A telephone-based self-management program for people with epilepsy. Epilepsy Behav 2009;14:232–6.
[27] McKenzie K, Chang YP. The effect of nurse-led motivational interviewing on medication adherence in patients with bipolar disorder. Perspect Psychiatr Care 2015;51:36–44.
[28] Michie S, Richardson M, Johnston M, Abraham C, Francis J, Hardeman W, et al. The behavior change technique taxonomy (v1) of 93 hierarchically clustered techniques: building an international consensus for the reporting of behavior change interventions. Ann Behav Med 2013;46:81–95.
[29] de Bruin M, Viechtbauer W, Schaalma HP, Kok G, Abraham C, Hospers HJ. Standard care impact on effects of highly active antiretroviral therapy adherence interventions: a meta-analysis of randomized controlled trials. Arch Intern Med 2010;170:240–50.
[30] Prochaska JO, Butterworth S, Redding CA, Burden V, Perrin N, Leo M, et al. Initial efficacy of MI, TTM tailoring and HRI's with multiple behaviors for employee health promotion. Prev Med 2008;46:226–31.
[31] Rollnick S, Mason P, Butler C. Health behavior change: a guide for practitioners. Churchill Livingstone; 1999.
[32] Moyers TB, Martin T, Manuel JK, Miller WR, Ernst D. Motivational interviewing treatment integrity 3.1.1: revised global scales. Albuquerque, NM: University of New Mexico; 2010.
[33] Easthall C, Song F, Bhattacharya D. A meta-analysis of cognitive-based behaviour change techniques as interventions to improve medication adherence. BMJ Open 2013;3.
[34] Pakpour AH, Gellert P, Asefzadeh S, Updegraff JA, Molloy GJ, Sniehotta FF. Intention and planning predicting medication adherence following coronary artery bypass graft surgery. J Psychosom Res 2014;77:287–95.
[35] Affolter N, Krahenbuhl S, Schlienger RG. Appropriateness of serum level determinations of antiepileptic drugs. Swiss Med Wkly 2003;133:591–7.
[36] Horne R, Weinman J, Hankins M. The beliefs about medicines questionnaire: the development and evaluation of a new method for assessing the cognitive representation of medication. Psychol Health 1999;14:1–24.

[37] Aflakseir A. Role of illness and medication perceptions on adherence to medication in a group of Iranian patients with type 2 diabetes. J Diabetes 2012;4:243–7.
[38] Schwarzer R, Antoniuk A, Gholami M. A brief intervention changing oral self-care, self-efficacy, and self-monitoring. Br J Health Psychol 2015;20(1):56–67.
[39] Scott-Lennox J, Bryant-Comstock L, Lennox R, Baker GA. Reliability, validity and responsiveness of a revised scoring system for the Liverpool Seizure Severity Scale. Epilepsy Res 2001;44:53–63.
[40] Cramer JA, Perrine K, Devinsky O, Bryant-Comstock L, Meador K, Hermann B. Development and cross-cultural translations of a 31-item quality of life in epilepsy inventory. Epilepsia 1998;39:81–8.
[41] Mohammadi N, Kian S, Davoudi F, Nia SM, Nojomi M. Psychometric evaluation of the Persian version of the quality of life in epilepsy inventory—31. Iran J Neurol 2013;12:144–8.
[42] Gollwitzer PM. Implementation intentions—strong effects of simple plans. Am Psychol 1999;54:493–503.
[43] Brown JM, Miller WR. Impact of motivational interviewing on participation and outcome in residential alcoholism treatment. Psychol Addict Behav 1993;7:211–8.
[44] Greineder DK, Loane KC, Parks P. Outcomes for control patients referred to a pediatric asthma outreach program: an example of the Hawthorne effect. Am J Manag Care 1998;4:196–202.
[45] La Greca AM, Schuman WB. Adherence to prescribed medical regimens. In: Roberts MC, editor. Handbook of pediatric psychology. 2nd ed. New York, NY: Guilford Press; 1995. p. 55–83 [xviii, 814].